Case Report:

Virilizing ovarian Leydig cell tumour

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ABSTRACT

Leydig cell tumours belong to the small group of ovarian steroid tumors, which are hormone producing and derived from specific stromal cells. Morphologically, their endocrine-like structure is characteristic, formed of large, polyhedral cells resembling luteal, adrenocortical and Leydig cells. They contain crystalloids of Reinke in their cytoplasm which have diagnostic significance. Patients with these tumours present with androgenic manifestations. We report the occurrence of Leydig cell tumour in a 35-year-old lady who presented with infertility and hirsutism.

Key Words: *Leydig cell tumour, Reinke's crystalloids*

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INTRODUCTION

Leydig cell tumours are rare and are usually benign. They belong to the group of ovarian steroid secreting tumours. They are hormone producing and derived from specific stromal cells. The ovarian steroid tumours are divided into subtypes according to their cell of origin as follows: (i) Stromal luteomas; (ii) Leydig cell tumours; and (iii) Steroid tumours not otherwise specified. The Leydig cell tumors have two forms; namely the hilus cell tumours which arise from preexisting normal Leydig cells of the hilus[1] and the stromal Leydig cell tumours, which take their origin in the cortex or subcortical region in the ovary from ovarian stromal cells that have differentiated into Leydig cells.[2] Leydig cells of different origin show the features of lipid cells and they contain crystalloids of Reinke. The presence of crystalloids is specific and of diagnostic value. We report the occurrence of Leydig cell tumour in a 35-year-old lady who presented with a history of infertility and signs of hirsutism and virilization.

CASE REPORT

A 35-year-old lady who was married for the last 15 years, presented for evaluation of infertility. On examination signs of hirsutism and virilization were noticed. Hair growth on the lower abdomen, scalp hair loss and clitoromegaly was noticed (Figures 1 and 2). She gave a history of experiencing regular

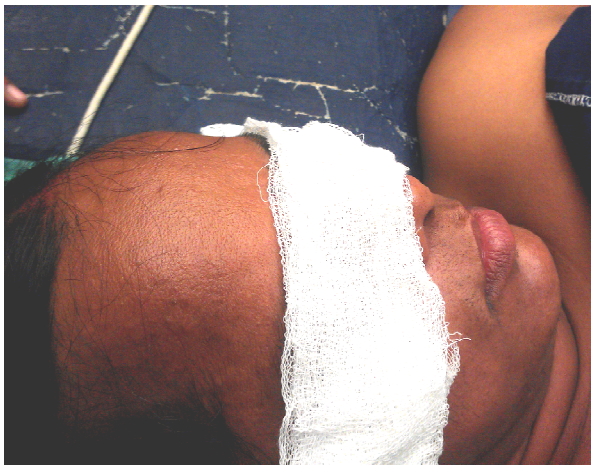

Figure 1: Clinical photograph showing frontal balding

Figure 2: Clinical photograph showing clitoromegaly

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menstrual cycles. No abdominal or pelvic adnexal masses were palpable.

Laboratory studies revealed a normal complete blood count and metabolic profile. Endocrinologic work up revealed normal hormone levels except for increased levels of total and free testosterone. Ultrasonography revealed a solid lesion measuring 2 × 2 × 1.5 cm in the right ovary; left ovary was normal. Exploratory laparotomy was done and bilateral salpingo-oophorectomy was performed. The specimen was sent for histopathological examination.

Grossly the right ovary showed a well circumscribed nodular mass measuring 2 × 1.5 × 1.5 cm with a grey yellow glistening cut-surface (Figure 3). Histopathological examination revealed tumour cells arranged in lobules separated by fibrous septa (Figure 4). The tumour cells were round to polygonal with abundant eosinophilic cytoplasm and round nuclei with prominent nucleoli (Figure 5). Few cells had vacuolated cytoplasm. Reinke's crystals were identified (Figure 6). These findings were suggestive of a Leydig cell tumour.

DISCUSSION

Most androgen secreting ovarian tumours are sex cord stromal tumors, which constitute less than 5% of all ovarian neoplasms.[3] According to the World Health Organization (WHO) histologic classification of ovarian tumours, sex cord stromal tumours can be classified as granulosa stromal cell tumours, Sertoli stromal cell tumours, mixed sex cord stromal tumours and steroid cell tumours.[4] Steroid cell tumours were also designated as "lipid cell tumours" but this term is not recommended because upto 25% of tumours in this category contain little or no lipid.[5] The term "steroid cell tumour" has been accepted by the WHO because it reflects both the morphological features of the neoplastic cells and their propensity to secrete steroid hormones.

Leydig cell tumours are rare ovarian steroid cell neoplasms composed entirely or predominantly of Leydig cells that contain crystals of Reinke. These tumors account for 15% to 20% of steroid cell tumours.[6] In the hilar zone, the Leydig cells can be normally found in 80% to 85% of the postpubertal ovaries, usually in association with non-myelinated nerve fibres. Hilar Leydig cell tumours arise from these preexisting Leydig cells of the hilus and can extend into the ovarian stroma depending on the size of the tumour.[6] These tumours are generally benign and are usually unilateral. The tumour size ranges between 1 and 15 cm in diameter but in majority of cases they are less than 5 cm. Macroscopically, they are solid, fleshy and well circumscribed. They appear yellow, orange or more commonly brownish in colour.[7] Reinke's crystals must be present to classify the tumour as Leydig cell tumour. These are elongated,

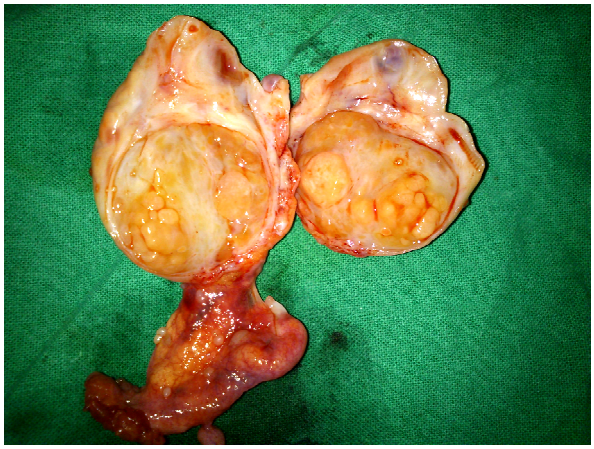

Figure 3: Operative specimen photograph of right ovary showing a well circumscribed nodular mass with grey yellow glistening surface

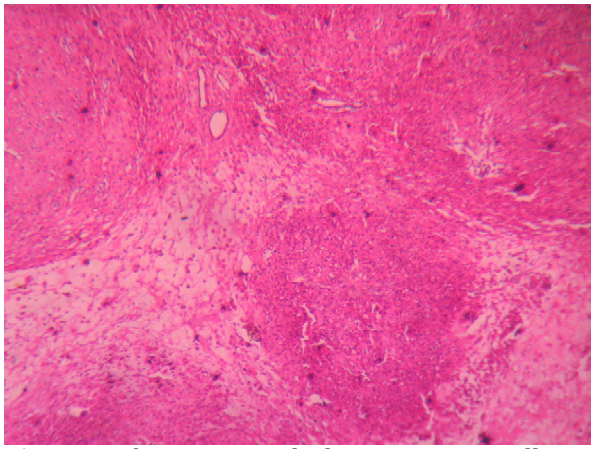

Figure 4: Photomicrograph showing tumour cells arranged in lobules separated by fibrous septa (Haematoxylin and eosin, × 100)

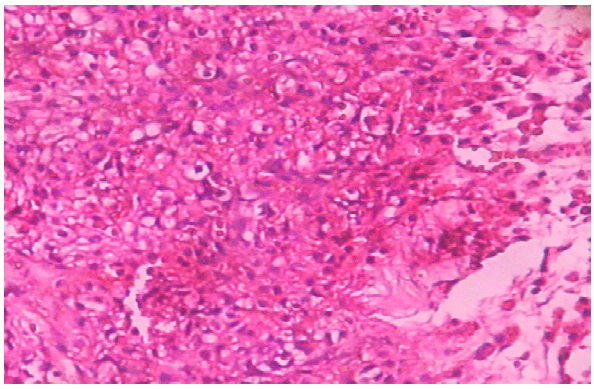

Figure 5: Photomicrograph showing round to polygonal tumour cells with abundant eosinophilic cytoplasm and round nuclei (Haematoxylin and eosin, × 600)

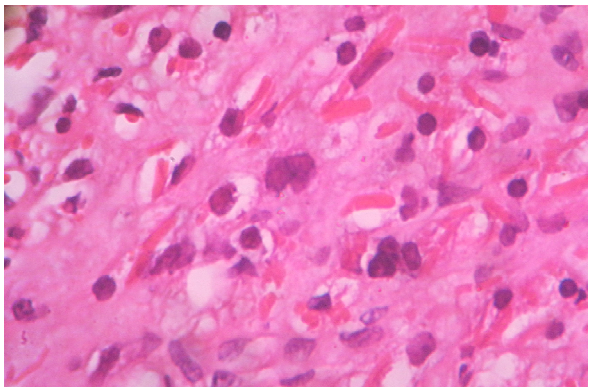

Figure 6: Photomicrograph showing tumour cells with Reinke's crystals (Haematoxylin and eosin, × 800)

hexagonal eosinophilic crystals present in the cytoplasm or rarely in the nucleus. In their absence, the tumour would be classified as a steroid cell tumour not otherwise specified. The Leydig cell tumour is mainly composed of diffusely arranged steroid cells with abundant eosinophilic cytoplasm, round hyperchromatic nuclei and sigle small nucleoli. Other notable features of a Leydig cell tumour include non medullated nerve fibres, the tendency for cells to cluster around vessels and fibrinoid necrosis of blood vessels walls.

Hilus cell tumours are encountered predominantly in postmenopausal women (average age 58 years) and cause hirsutism and/or virilization in 75% of cases. These tumours secrete testosterone and occasionally oestrogenic activity may be observed. The androgenic manifestations are milder than those associated with Sertoli-Leydig cell androblastomas and their onset is less abrupt. Patients with these tumours usually present with signs of virilization, including severe hirsutism, frontal balding, clitoromegaly, increased libido, altered body fat, increased muscle mass, breast atrophy, deepening of voice and pustular acne.[6] Oestrogenic manifestations, such as irregular menses or postmenopausal bleeding have also been reported.[8]

The stromal-Leydig cell tumours take their origin in the cortex or subcortical region in the ovary from ovarian stromal cells, which have differentiated into Leydig cells. They are very rare benign tumours. Like hilus tumours they also occur in postmenopausal patients and are unilateral. Macroscopically these tumours are multinodular and lobulated and have greatest dimensions of two to five cms. Microscopic examination show nests of Leydig cells admixed with ovoid and spindle shaped cells, which show the appearances of stromal hyperthecosis or thecoma. Presence of detectable crystalloid of Reinke is required for identification of Leydig cells of stromal origin.

The differential diagnosis of the Leydig cell tumours includes ovarian neoplasms containing Leydig cells or luteinized stromal cells. Sertoli-Leydig cell androblastoma occasionally exhibits predominance of Leydig cell component. But presence of Sertoli cells excludes the diagnosis of pure Leydig cell neoplasm. Luteinized stromal cells are very much similar to the Leydig cells but the presence of Reinke's crystalloids help in the diagnosis. Stromal luteoma is a distinct type of steroid tumours arising in the ovarian stroma which resembles Leydig cell neoplasms. Grossly both the tumours are indistinguishable but the presence of crystalloids helps in the correct diagnosis.

Androgen producing tumours should be suspected in women with virilizing clinical symptoms and high testosterone levels. Sertoli

Leydig cell tumours are larger and usually found easily on imaging, whereas hilar Leydig cell tumours are smaller and often difficult to find on imaging. If clinical suspicion is high exploratory laparotomy is indicated. It is noteworthy that in this era where sophisticated and expensive histopathological methods including immunohistochemistry are available, this rare and benign tumour can be diagnosed with high accuracy on good quality haematoxylin and eosin stained slides.

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